

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 10159 -- PCT	<b>FOR FURTHER ACTION</b>		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US05/00638	International filing date (day/month/year) 07 January 2005 (07.01.2005)	(Earliest) Priority Date (day/month/year) 07 January 2004 (07.01.2004)	
Applicant BRISTOL-MYERS SQUIBB COMPANY			

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the language, the international search was carried out on the basis of:



the international application in the language in which it was filed.



a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☒ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box No. II)

3. ☒ Unity of invention is lacking (See Box No. III)

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

[Faint, illegible text]

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

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## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



on paper



in electronic form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☐

In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3.

Additional comments:

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## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-in-part, 3, 3-in-part

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12Q 1/00( 2006.01),1/68( 2006.01)  
C07K 1/00( 2006.01)

USPC: 435/4,6,7.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 435/4, 6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	NORMANNO et al. Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors (EGFR-TKIs): Simple Drugs with a Complex Mechanism of Action. J. Cell. Physiol., 2002. Vol 194, pgs 13-19, see especially pages 13, 14, 19.	1,-in-part, 2, 3
Y	WONG et al. Identification of Liver-Intestine Cadherin in hepatocellular carcinoma-a potential disease marker. BBRC. 2003. Vol 311. pgs 618-624, see especially the abstract, pgs 619 and p. 623.	1-in-part, 2, 3-in-part
Y	SLESAC et al. Expression of epidermal growth factor receptor family proteins (EGFR, cerB-2 and c-erbB-3) in gastric cancer and chronic gastritis. Anticancer Res., Jul-Aug 1998. Vol. 18. No. 4A. pgs 2727-2732, see especially the abstract.	1-in-part, 2, 3-in-part

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
03 July 2007 (03.07.2007) ✓

Date of mailing of the international search report

Name and mailing address of the ISA/US  
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### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group 1, claims 1-in part, 2, 3-in-part drawn to a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises measuring in the mammal the level of SEQ ID NO:1, cadherin 17, wherein a difference in level of SEQ ID NO:1 is indicative that the mammal will respond to said method of treating cancer.

Groups 2-125, claims 1-in part, 2, 3-in-part drawn to a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises measuring in the mammal the level of at least one biomarker selected from the 125 biomarkers disclosed in Table 1, other than SEQ ID NO:1, cadherin 17 wherein a difference in said biomarker or combination of biomarkers is indicative that the mammal will respond to said method of treating cancer. Additional fees must be paid for the search for the claimed method using of each individual biomarkers or biomarkers in combination.

A international stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features which define a contribution over the prior art. If there is no special technical feature, if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(d). After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).)

An international stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. When claims to different categories are present in the application, the claims will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) A product and a process specially adapted for the manufacture of said product; or (2) A product and a process of use of said product; or (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or (4) A process and an apparatus or means specifically designed for carrying out the said process; or (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(b) and (d). Group 1 will be the main invention. After that, all other products and methods will be broken out as separate groups (see 37 CFR 1.475(d).)

Group 1 is drawn to a method for identifying a mammal that will respond therapeutically to a method of treating cancer comprising administering an EGFR modulator, wherein the method comprises measuring in the mammal the level of SEQ ID NO:1, cadherin 17, wherein a difference in level of SEQ ID NO:1 is indicative that the mammal will respond to said method of treating cancer.

Groups 2-125 do not form a single inventive concept with the invention of Group 1 because they are drawn to additional methods and products used in those methods..

Accordingly, Groups 1-125 are not so linked as to form a single general inventive concept.

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Continuation of B. FIELDS SEARCHED Item 3:

GENBANK, MEDLINE

search terms:SEQ ID NO:1, cadherin, cancer gastric, liver, EGFR

